

POINTS TO CONSIDER

Protocol: Intensive Immunosuppression Followed by Rescue with CD34 Selected, Leukopheresis Products in Patients with Multiple Sclerosis

SCIENTIFIC ABSTRACT

There has been much interest lately in the use of hemopoietic stem cell transplantation as therapy for autoimmune disease. The initial rationale for this approach comes from reports showing clinical improvement of autoimmune diseases in patients undergoing allogeneic transplantation for a coexisting malignancy. There are also several anecdotal reports of patients with autoimmune disorders who underwent autologous transplantation for another disorder and experienced remission of their auto-immune disorder although most have eventually relapsed. However, the majority of these patients received unmanipulated products.

The mechanism by which transplant mediates a beneficial effect may involve removal of the autoreactive T cell clone by the conditioning regimen and a resetting of the immune system derived from infused cells. With the availability of CD34 selection devices, investigators can positively select stem cells and then perform further T depletion procedures to ensure autoreactive cells are not reinfused. The ultimate aim is to regenerate an intact non-immunoreactive immune system. One concern with this strategy is that prolonged immunodeficiency may occur because regeneration is slow resulting in an increased risk of viral infection and malignant disease.

A critical issue is therefore how to obtain recovery of normal immunity without resurgence of autoimmune disease. A prerequisite for this aim is to identify the source of regeneration, so that appropriate means can be utilized to enhance normal recovery. With current autologous protocols in patients with autoimmune diseases, it is unclear whether the regenerating immune system derives from the infused graft or from regenerating cells in the host. Moreover, should autoreactive clones again develop there is no means of determining if they are regenerating from infused or residual cells. We propose to address these issues by using a gene marking technique that we have previously used to track infused cells after transplantation.